

# Atom Equivalents for Converting DFT Energies Calculated on Molecular Mechanics Structures to Formation Enthalpies

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**ABSTRACT:** New atom equivalents are introduced to convert BP/DN\*\*//MMFF energies into formation enthalpies. As a result of using molecular mechanics structures, poor results are obtained for compounds outside the scope of the force field, such as those bearing  $\text{—NF}_2$  groups or some nitrogenous systems. Notwithstanding these limitations, present procedures compare well with the results of previous atom equivalents schemes. Indeed, rms deviations from experiment are below 9 kJ/mol for hydrocarbons, and close to 16 kJ/mol for a variety of compounds reasonably well described by MMFF. The explicit inclusion of thermal and vibrational contributions, using calculated frequencies, does not improve the results. This study demonstrates that cost-effective approaches to formation enthalpies may be developed on the basis of a combination of DFT with a suitable molecular mechanics force field.  
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## Introduction

There is considerable practical interest in the determination of thermodynamic properties of molecules from calculations.<sup>1,2</sup> The cost and waste associated with the design of new materials are reduced if some compounds may be ruled out on the basis of calculated relevant properties. In the field

of propellants, a fast, widely applicable and reliable procedure is needed to estimate the amount of energy stored in such materials. For this purpose, gas phase formation enthalpies  $\Delta_f H^\circ$  are required, in addition to sublimation enthalpies  $\Delta_{\text{sub}} H^\circ$ . In view of the performance of currently available models to estimate  $\Delta_{\text{sub}} H^\circ$ ,<sup>3</sup> very accurate calculations of  $\Delta_f H^\circ$  are pointless. Moreover, the cost of such calculations might be prohibitive for many molecules of interest. However, standard semiempirical methods commonly used in the field of energetic

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materials do not provide the target accuracy required to discriminate between high-energy candidate compounds.<sup>4–6</sup> Introducing *ad hoc* corrections to AM1 or PM3 enthalpies is questionable as those methods are already calibrated against  $\Delta_f H^\circ$  values.<sup>6</sup> Thus, there is a need for more reliable techniques to estimate  $\Delta_f H^\circ$ .

In some cases, very accurate values may be obtained using group contribution methods,<sup>7</sup> bond energy schemes,<sup>8</sup> or molecular mechanics force fields such as those developed by Allinger and coworkers.<sup>9–11</sup> However, the scope of such methods is limited by the number of parameters involved. For instance, in addition to the MM3 force-field parameters describing interatomic forces, accurate evaluations of  $\Delta_f H^\circ$  also require specific bond-energy increments and structural parameters for every new class of compounds investigated. This approach, based on extensive experimental data, gives excellent results for hydrocarbons,<sup>11,12</sup> aliphatic and aromatic nitro compounds,<sup>13</sup> alcohols and ethers,<sup>14</sup> nitrogen-containing aromatic heterocycles,<sup>15</sup> furan, vinyl ethers, and related compounds,<sup>16</sup> or sulfur-nitrogen heterocycles.<sup>17</sup> However, application of this method to new compounds requires derivation of additional parameters.<sup>18</sup> Despite some attempts at facilitating this task,<sup>18,19</sup> it remains difficult, and may be hampered by a lack of experimental data. As a result, this approach cannot be routinely applied to arbitrary organic compounds.

The PIMM force field<sup>20</sup> depends on much fewer parameters and can, therefore, be assessed for a wider range of compounds. Although recent results<sup>5</sup> indicate that it is superior to AM1 and PM3 with regard to the prediction of  $\Delta_f H^\circ$ , more reliable procedures are still desirable to optimize the selection of chemical structures on the basis of their theoretical performances.

Turning to a first-principles description of the electronic structure and molecular energy is the natural step to overcome the practical limitations associated with heavy parameterization. To derive satisfactory values of  $\Delta_f H^\circ$  at reasonable cost, the Hartree–Fock (HF) or Density Functional Theory (DFT) methods are the main alternatives. At the HF level, it is well known that accurate reaction enthalpies are obtained only for isodesmic reactions.<sup>21</sup> However, systematic errors due to the neglect of electron correlation can be corrected using atom or group equivalents.<sup>22</sup> Such empirical corrections have been quite successful to estimate  $\Delta_f H^\circ$  from HF calculations.<sup>23–25</sup> More recently, atom equivalents (AEs) have been found useful to estimate

better  $\Delta_f H^\circ$  from DFT.<sup>26–28</sup> So far, much work concerned with the application of some variant of the AE approach to either HF or DFT energies has focused on alkanes or other hydrocarbons, for which a very good accuracy could be obtained. For instance, Mole et al. reported a rms deviation from experiment of 4.3 kJ/mol for hydrocarbons using B3LYP energies.<sup>27</sup> Restricting their attention to alkanes and introducing additional adjustable parameters, Labanowski et al.<sup>29</sup> reported a rms deviation as small as 1.6 kJ/mol. Provided a sufficient number of parameters are introduced, good results can be obtained on the basis of *ab initio* calculations<sup>30</sup> and for other classes of organic compounds, for example, aldehydes and ketones.<sup>31</sup> However, with regard to the simple AE procedures involving few parameters, recent investigations indicate a significant loss of accuracy on going to molecules with heteroatoms.<sup>26,28</sup> Using a procedure very similar to that of Mole et al.,<sup>27</sup> Rice et al.<sup>28</sup> reported a rms error close to 13 kJ/mol for a set of energetic compounds, while similar calculations relying on the BP functional yielded a rms deviation close to 17 kJ/mol.<sup>26</sup> Nevertheless, those results are better than those obtained using semi-empirical approaches,<sup>4–6,32</sup> and useful with regard to predicting the performance of energetic materials. The aim of the present article is not to strive for chemical accuracy, but rather to suggest more efficient procedures.

In the above-mentioned AE approaches, most computational effort is spent to optimize the molecular geometry. It is well established that the calculation of total energies requires higher theory levels than geometry optimization.<sup>33</sup> Therefore, the use of hybrid procedures to derive  $\Delta_f H^\circ$  might offer substantial time savings. Accordingly, Herndon reported excellent results for hydrocarbons on the basis of HF/6–31G\* energies calculated on HF/STO-3G equilibrium structures.<sup>24</sup> More efficient versions of available general procedures<sup>26,28</sup> could probably be developed without significant loss in accuracy using this strategy. In view of the computational data reported by Foresman and Frisch,<sup>33</sup> DFT energies calculated on semiempirical AM1 structures are only slightly less reliable than those obtained through energy minimization at the DFT level. On the other hand, recent progress in force-field development warrant the use of molecular mechanics to calculate equilibrium geometries. Therefore, it seems worth investigating how much the accuracy of calculated  $\Delta_f H^\circ$  is affected by going from the quantum mechanical to the molecular mechanics geometry, as the use of the latter allows dramatic time savings.

This is precisely the purpose of the present article. The specific procedures employed to convert energies into formation enthalpies are outlined, followed by further computational details. After a comparison of molecular mechanics and DFT geometries, new atom equivalents are derived. Finally, they are used to calculate formation enthalpies. In view of our interest in practical and widely applicable methods, the results are especially compared with the values reported by Habibollahzadeh et al.<sup>26</sup> and Rice et al.<sup>28</sup> For simplicity, the procedure and the set of molecules used in ref. 26 are hereafter denoted HGCMP.

## Theory

Statistical mechanics tells us how to derive standard formation enthalpies  $\Delta_f H^\circ$  from molecular mechanics<sup>9,34</sup> or quantum mechanical calculations.<sup>35</sup> Allinger and coworkers<sup>31,35</sup> have shown that chemical accuracy could be obtained provided a sufficient number of parameters are introduced to allow the fine tuning of the calculation. For this work, a more approximate equation involving few adjustable parameters is desirable. A useful scheme based on the thermodynamic cycle shown in Figure 1 consists of calculating the enthalpy change upon going from the separated elements to the molecule, using available experimental values for the formation enthalpies  $H_K^\circ$  of the gaseous atoms.<sup>36</sup> As mentioned in the introduction, this straightforward approach yields poor results in practice because the reaction involved is generally not isodesmic. Therefore, one must resort to AEs  $X'_K$  to make up for the systematic errors affecting the calculated molecular energy; hence, the following

equation for  $\Delta_f H^\circ$ :

$$\Delta_f H^\circ = E + ZPE + TR + ROT + VIB + kT + \sum_K H_K^\circ + \sum_K X'_K \quad (1)$$

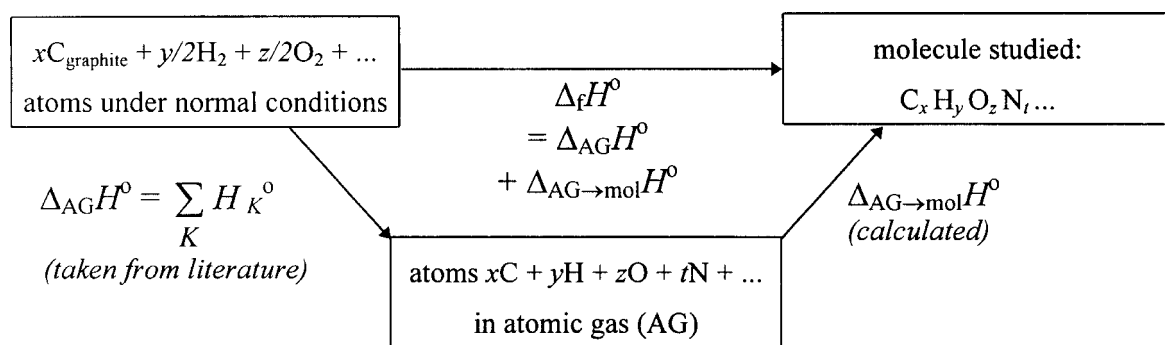
where the sums run over all atoms with serial index  $K$ . The equilibrium energy  $E$  may be obtained from quantum chemistry codes. Harmonic vibrational frequencies can be used to estimate the zero-point energy  $ZPE$ , as well as translational, rotational, and vibrational thermal energies  $TR$ ,  $ROT$ , and  $VIB$ , respectively. The term  $kT$  converts energy into enthalpy. The correction terms  $X'_K$  can be obtained from a least-squares fit of reliable experimental data. This procedure was employed by Habibollahzadeh et al.<sup>26</sup> Conceptually, it consists of two stages: first, the calculation of a theoretical uncorrected value for  $\Delta_f H^\circ$ ; then the addition of the correction terms  $X'_K$ . The latter not only accounts for the deficiency of the quantum mechanical model used to calculate the energy  $E$ , but also for the lack of explicit corrections for anharmonicity or high-energy conformations.

## THE P1 PROCEDURE

In practice, it is convenient to merge the two stages mentioned above, including the atomic formation enthalpies  $H_K^\circ$  in new empirical parameters  $X_K$  as follows:

$$\Delta_f H^\circ = E + ZPE + TR + ROT + VIB + kT + \sum_K X_K \quad (2)$$

The values of the new AEs  $X_K$  are, of course, much larger than the correction terms  $X'_K$ , as they include the (positive) formation enthalpies of the isolated atoms. This procedure is hereafter denoted as P1. It is clearly equivalent to that relying on eq. (1).



**FIGURE 1.** Thermochemical cycle illustrating the use of experimental atomic data combined with the theoretical enthalpy change associated with the formation of the molecule from its separated elements.

## THE P2 PROCEDURE

In view of the relatively high computational cost associated with the evaluation of the vibrational frequencies, it is convenient to include *ZPE + VIB* in the AEs. Indeed, the vibrational energy can be expressed in terms of atomic contributions with very good accuracy.<sup>37</sup> On the other hand, accounting explicitly for the remaining temperature-dependent contribution does not yield any practical gain unless very high levels of theory are used. For instance, the results obtained by Mole et al.,<sup>27</sup> using the B3LYP functional, are slightly worse if those terms are taken into account. Thus, it is a usual practice<sup>20,22,23,27</sup> to use the following approximation:

$$\Delta_f H^\circ = E + \sum_K Y_K \quad (3)$$

The procedure introduced in the present article on the basis of eq. (3) is hereafter denoted P2.

The distinctive feature of both P1 and P2 procedures used in the present work stems from the fact that they rely on DFT energies  $E$  calculated on molecular mechanics structures. As the computer demands of the latter are negligible when compared to the requirements of quantum methods, the time needed to estimate  $\Delta_f H^\circ$  is reduced by one or even two orders of magnitude with respect to more conventional approaches.<sup>22–31</sup> In addition, convergence problems often encountered during the optimization stage for large systems with soft modes can be avoided or fixed more easily.

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## Computational Approach

### THE FORCE FIELD

Molecular mechanics parameterization for nitrogenous compounds proves challenging.<sup>38</sup> Although the MM3 force field has been successfully applied to nitrogen heterocycles<sup>15,17</sup> or simple nitro compounds,<sup>13</sup> the fact that it provides thermally averaged geometries—as measured from electron diffraction experiments—rather than equilibrium structures—as obtained from *ab initio* calculations—makes the comparison with previous work more difficult. In the present work, the MMFF force field is employed.<sup>39</sup> This choice is mainly dictated by the wide coverage of organic compounds provided by its core parameterization, and by its fair reliability with regard to geometries and frequencies.<sup>40</sup> In contrast to many alternative force fields, MMFF is mostly parameterized against computational data,

a desirable feature to facilitate comparisons with earlier work based on structures optimized at the DFT level.<sup>26–28</sup>

Nonetheless, some limitations of MMFF should be kept in mind. For instance, some problems regarding the geometry of nitrogen in amides and unsaturated amines have been reported.<sup>40</sup> Moreover, despite the large number of chemical families treated in the core parameterization of the force field, some parameters are still missing for many compounds of interest. Therefore, in addition to the core parameters, an extended parameterization employing generic parameters and empirical rules is provided.<sup>41</sup> It is of interest to investigate the performance of MMFF when applying this extension to energetic molecules. Preliminary results of such studies are reported below, before addressing the problem of formation enthalpies.

Although MMFF may provide rather good geometries and frequencies, it is worth noting that MMFF steric energies are not suitable to derive  $\Delta_f H^\circ$ ; hence, the necessity of subsequent single-point calculations. This fact is well illustrated by the large difference (>250 kJ/mol) between the MMFF energies of pyrazine and pyrimidine. Because the AEs associated with both isomers are the same, any AE-based method would predict striking differences between their  $\Delta_f H^\circ$  values, in sharp contrast with the experimental values of 196.1 and 195.8 kJ/mol.<sup>42</sup>

### THE DFT MODEL

Molecular energies are obtained through single-point DFT calculations on MMFF structures, using the BP gradient-corrected functional<sup>43</sup> with the DN\*\* numerical basis set.<sup>44,45</sup> Comparisons of the present results with those derived from eq. (1) using DFT equilibrium structures<sup>26</sup> allow one to assess the effect of replacing BP/DN\*\* by MMFF for the geometry optimization.

### DETERMINATION OF THE ATOM EQUIVALENTS

With regard to equilibrium structures, the BP functional yields systematic errors<sup>46</sup> that differ from those obtained using the MMFF force field. The resulting differences between BP/DN\*\* and BP/DN\*\*//MMFF energies obviously affect the optimal values of the AEs, thus warranting a re-optimization of these equivalents to make up for the systematic discrepancies between MMFF and BP/DN\*\* geometries. Through the development of specific BP/DN\*\*//MMFF AEs, the accuracy of the

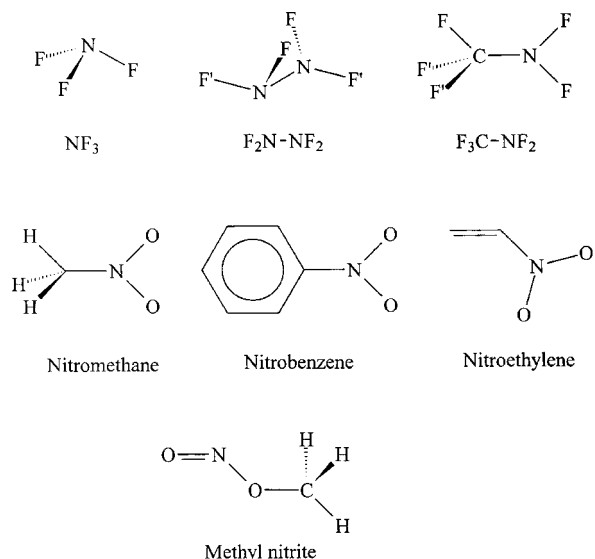
HGCMP scheme<sup>26</sup> might be retained, at least for the molecules well within the scope of the force field. In addition, as suggested by those authors,<sup>26</sup> an expanded database is used to enhance the reliability of the AEs, including 86 simple compounds made of H, C, N, O, F, and Cl atoms in a variety of environments.<sup>47</sup>

## FURTHER COMPUTATIONAL DETAILS

Molecular mechanics and DFT calculations were carried out with the Spartan program<sup>48</sup> using the fine integration mesh. The semiempirical PIMM results were obtained using the 1991 version of the program.<sup>49</sup> In any case, default convergence criteria were retained for SCF iterations and geometry optimization. The latter is stopped when the maximum residual force is smaller than  $3 \cdot 10^{-4}$  a.u. As the magnitude of cartesian force constants is typically 1 a.u., it is clear that further optimization of the geometry would result in no significant change of the total energy.

## Influence of Using MMFF Geometries

A detailed discussion of MMFF vs. DFT geometries is beyond the scope of this article. However, preliminary results are reported to compare MMFF and DFT structures for the HGCMP panel and additional compounds not covered in the core parameterization of the force field. To our knowledge, further assessment of the performance of the MMFF force field remains to be done, especially with regard to the extended parameterization based on empirical rules. The original articles do not provide a definite conclusion, as the equilibrium geometries are mostly compared to X-ray structures.<sup>40</sup> Ideally, comparisons of calculated structures against experiment requires converting all geometric parameters into the same kind of data, using the methods introduced by Ma et al.<sup>50</sup> For the sake of comparison with results obtained using DFT structures,<sup>26–28</sup> MMFF structures reported here are compared with DFT geometries optimized at the BP/DN\*\* level. The poor MMFF geometries found in some cases account for the most severe discrepancies obtained in the present work between calculated and measured values of  $\Delta_f H^\circ$ . Accordingly, the most severe breakdowns of the extended MMFF parameterization are reported below. Two classes of compounds are especially concerned—namely nitroaromatic compounds and those showing N—F bonds. They are shown in Figure 2, and their geometries are reported in Table I.



**FIGURE 2.** Molecules poorly described with the MMFF force field (nitromethane is listed for the sake of comparison). Hydrogen atoms not shown for nitrobenzene and nitroethylene.

## NITRO COMPOUNDS

As mentioned by Allinger et al.,<sup>13</sup> the prediction of the geometry of the nitro group on aliphatic moieties is a tricky problem because it may then be considered as a free rotor.<sup>51</sup> Thus, only bond lengths and bond angles are reported in Table I. For nitromethane, the C—NO<sub>2</sub> bond length predicted by the MMFF force field is smaller than the DFT value by  $\sim 0.02$  Å, i.e., in very good agreement with the experimental value of 1.489 Å.<sup>52</sup> Moreover, the N—O bond length and the ONO angle are close to the experimental values of 1.224 Å and 125.3 degree.<sup>52</sup> For nitroaromatics, in the lack of steric hindrance, the nitro group lies in the plane of the ring.<sup>53</sup> However, MMFF predicts the nitro group to lie perpendicular to the aromatic ring. Similarly, instead of the planar structure, the nitro group of nitroethylene in the MMFF equilibrium structure is perpendicular to the vinylic moiety. Considering the values of the rotational energy barriers,<sup>54</sup> BP/DN\*\*//MMFF energies should be larger than true BP/DN\*\* values by only 10–20 kJ/mol. In fact, in addition to the spurious orientation of the nitro group, MMFF yields dramatically underestimated C(*sp*<sup>2</sup>)—NO<sub>2</sub> bond lengths, as indicated in Table I. With respect to the BP/DN\*\* values, the difference is as large as 0.110 and 0.132 Å for nitrobenzene and nitroethylene, whereas typical errors of MMFF with respect to experiment are below 0.02 Å within the core parameterization.<sup>39</sup> Therefore, although the structure obtained for ni-

**TABLE I.**  
**MMFF versus BP/DN\*\* Geometric Parameters (Å and Degrees) as Defined from Figure 2.**

		MMFF	BP/DN**
NF <sub>3</sub>	N—F	1.227	1.410
	F—N—F	110.4	101.5
F <sub>2</sub> N—NF <sub>2</sub>	N—N	1.425	1.535
	N—F	1.227	1.409
	N—F'	1.227	1.405
	N—F—N'	110.5	103.0
	N—N—F	111.0	107.0
	N—N—F'	110.7	99.8
	F—N—N—F'	64.0	67.6
H <sub>3</sub> C—NF <sub>2</sub>	C—N	1.450	1.518
	N—F	1.227	1.416
	C—F	1.355	1.339
	C—F'	1.354	1.337
	F—N—F	110.3	103.0
	F—N—C	111.2	103.2
Nitromethane	C—N	1.487	1.508
	N—O	1.237	1.234
	C—N—O	117.0	117.6
	O—N—O	125.9	125.8
Nitrobenzene	C—N	1.380	1.489
	N—O	1.239	1.237
	C—N—O	117.6	117.5
	O—N—O	124.8	125.0
	C—C—N	119.7	119.0
Nitroethylene	C—N	1.343	1.475
	N—O	1.237	1.236
	N—O'	1.237	1.241
	C—N—O	117.3	119.1
	C—N—O'	117.3	115.4
	O—N—O	125.4	125.6
Methyl nitrite	C—O	1.423	1.443
	O—N	1.263	1.483
	N=O	1.235	1.180
	C—O—N	109.2	108.6
	O—N=O	111.0	110.5
	N—O—C—H	179.9	176.1
	O=N—O—C	133.0	–179.1

tromethane suggest a fair description of nitroalkanes, the MMFF force field is clearly not suitable for studies of nitroaromatic compounds.

### FLUORINE–NITROGEN BONDS

Another chemical family for which MMFF completely fails to provide reasonable geometries is that of the NF<sub>3</sub>, F<sub>2</sub>N—NF<sub>2</sub> and F<sub>3</sub>C—NF<sub>2</sub> compounds (see Fig. 2). As shown in Table I, rms deviations as large as 0.137 Å and 7.6 degrees are observed for bond lengths and angles, i.e., 10 and 6 times, respec-

tively, as large as standard deviations reported by Halgren.<sup>40</sup> The problem arises because MMFF predicts too short N—F bonds, with deviations as large as 0.18 Å. Accordingly, it is not surprising that the angles at the nitrogen are overestimated to accommodate the steric hindrance of fluorine atoms. This complete breakdown of MMFF for N—F bonds is reminiscent of the very poor H—F bond length reported for hydrogen fluoride.<sup>45</sup> Thus, despite the good results obtained for HF or NF<sub>3</sub> on the basis of the Schomaker–Stevenson rule used by the extended MMFF parameterization,<sup>55</sup> the latter is not suitable for those structures. On the other hand, the length of the central bond in F<sub>2</sub>N—NF<sub>2</sub> is too short by 0.11 Å. In view of these severe errors, it is clear that no accurate  $\Delta_f H^\circ$  can be calculated on MMFF structures for such compounds.

### BP/DN\*\*//MMFF VS. BP/DN\*\* ENERGIES

Before embarking on the development of a new set of atom equivalents, DFT energies conventionally obtained on DFT-optimized structures (BP/DN\*\* values) are now compared with those calculated on the MMFF structures (BP/DN\*\*//MMFF values) for the HGCMP panel.<sup>26</sup> As expected from previous results concerning geometries, the largest deviations occur for nitrogenated compounds, especially those bearing nitro or nitrite groups. Indeed, with respect to BP/DN\*\* values, BP/DN\*\*//MMFF energies are overestimated by 80 kJ/mol for methyl nitrite, 68 kJ/mol for TATB (triaminotrinotrobenzene) and 48 kJ/mol for nitroaniline. The rms deviation between BP/DN\*\* and BP/DN\*\*//MMFF energies is 18 kJ/mol. Because the rms deviation of HGCMP enthalpies from experiment is close to 17 kJ/mol,<sup>26</sup> and considering the fact that some systematic changes in total energies associated with the use of MMFF structures may be absorbed into the atom equivalents, the use of MMFF structures could broaden the scope of the HGCMP scheme<sup>26</sup> or similar approaches<sup>28</sup> to larger compounds and/or more extensive studies with no significant loss of accuracy.

### Atom Equivalents

The AEs  $X_K$  and  $Y_K$  derived from the calibration panel (Table II) and associated with the P1 and P2 procedures, respectively, are listed in Table III. Their different magnitudes reflect the inclusion of thermal and zero-point contributions in the  $Y_K$ . These AEs are allowed to depend on the hybridization, following the work of Habibollahzadeh et al.<sup>26</sup> However,

**TABLE II.** Calibration Panel Used to Derive the Atoms Equivalents Listed in Table III.

	P2	$\Delta$
2,2,3,3-Tetrafluoro-1-propanol	-1061.3	7.3
Hexafluorobenzene	-956.0	-2.5
Tetrafluoromethane	-933.2	18.6
Pentafluorobenzene	-806.0	-4.0
Chlorotrifluoromethane	-707.9	7.9
Trifluoromethane	-697.1	4.0
1,2,4,5-Tetrafluorobenzene	-646.8	-11.0
3-Methyl-butanoic acid	-510.0	1.0
Trifluoroacetonitrile	-497.9	7.2
Butanoic acid	-475.9	-10.9
Chlorodifluoromethane	-482.0	-4.0
2,3-Butanediol	-482.3	22.4
Difluoromethane	-450.7	-3.2
1,2,4-Benzenetriol	-444.0	-8.4
Propyl formate	-462.7	33.1
Methyl acetate	-410.0	-15.1
1,4-dioxane	-315.3	-18.1
Hexanol	-315.9	-10.2
Cyclohexanol	-286.2	-8.1
2-Propanol	-272.6	-3.4
Acetamide	-238.3	-15.8
Urea	-235.5	-13.6
Ethanol	-243.8	3.1
Cyclopentanol	-242.5	2.0
Fluoromethane	-234.3	-1.7
Acetone	-217.1	-6.1
<i>N,N</i> -Dimethyl-formamide	-192.4	-22.3
Formamide	-186.0	-23.2
Propanal	-185.6	-10.0
2,2,3-Trimethyl-butane	-204.5	16.0
2,2-Dimethyl-butane	-185.6	9.9
Ethanal	-166.2	-5.6
2-Methyl-2-nitro-propane	-177.1	5.4
2,3-Dimethyl-butane	-177.8	6.2
Neopentane	-167.9	0.6
Hitrobutane	-143.9	-15.9
2-Methyl-butane	-153.7	-3.7
1-Fluoro-4-methylbenzene	-147.5	0.7
Isobutane	-134.2	-4.2
Ethoxy-ethene	-140.8	3.0
<i>n</i> -Butane	-127.1	-7.2
Cyclohexane	-123.4	-7.7
Cyclooctane	-124.4	2.6
Cycloheptane	-118.1	-2.3
Chloroethane	-124.5	4.3
Nitroethane	-102.3	-14.4
Propane	-104.7	-9.3
Formaldehyde	-115.9	8.1
Chloroform	-103.2	-1.3
Butylamine	-91.9	-5.3
Ethane	-83.7	-7.3
Methyl chloride	-83.7	-3.9

**TABLE II.** (Continued)

	P2	$\Delta$
Hydrogen chloride	-92.3	6.9
Cyclopentane	-76.4	-5.6
Phenol	-96.4	14.6
Methane	-74.5	-0.9
2-Methyl-1,2-propanediamine	-90.3	18.1
Dinilromethane	-58.9	12.4
Methylamine	-22.5	-2.2
Dimethylamine	-19.5	-5.0
Tetrachloroethylene	-12.4	1.4
1,2,3-Trimethylbenzene	-9.5	2.3
<i>p</i> -Xylene	18.0	-0.9
2-Methyl-propanenitrile	23.4	-5.0
Butanenitrile	33.6	-15.0
1,2-Dimethylbenzene	19.1	0.1
Cyclobutane	28.4	-8.3
1,3-Dimethylbenzene	17.3	3.6
Acetalimine	24.0	9.2
Propanenitrile	51.7	-9.7
Methylbenzene	50.4	-2.0
Chlorobenzene	51.8	-1.2
Ethanenitrile	74.0	-12.0
Ethylenediamine	84.1	-10.8
Cyclopropylamine	77.0	-1.3
Benzene	82.9	-3.0
<i>N</i> -Methyl methanimine	44.0	39.2
4-Methyl-pyridine	103.8	-12.0
1H-Imidazole	139.3	-25.7
Hydrogen cyanide	135.1	-4.2
1H-Pyrazole	179.4	-30.3
Butyne	165.2	-0.1
Dimethyl-diazene	148.6	26.1
Propyne	184.9	0.1
4-Pyridinecarbonitrile	283.5	-19.5
Acridine	273.9	12.8
Bicyclo[1.1.0]butane-1-carbonitrile	304.5	38.6
rms		12.6

For every molecule are reported in kJ/mol the formation enthalpy  $\Delta_f H^\circ$  obtained from the P2 procedure and the error  $\Delta$  with respect to the experimental value.<sup>47</sup>

these authors introduced two different values for trivalent nitrogen, according to whether the geometry of the atom is planar or pyramidal. This may lead to some ambiguities because many nitrogens, especially in amides, are more or less puckered according to the level of theory used, while observed geometries are essentially planar owing to vibrational averaging. In this context, the fact that predicted values of  $\Delta_f H^\circ$  are modified by more than 33 kJ/mol upon going from the pyramidal to the

**TABLE III.**  
**Group Equivalents  $X_K$  and  $Y_K$  Derived in View of**  
**Applications with Procedures P1 and P2,**  
**Respectively (kJ/mol).**

Atom Type	Coord.	$X_K$	$Y_K$
H	1	1534.4	1557.6
C	4	100,090.2	100,114.9
C	3	100,101.1	100,119.5
C	2	100,103.4	100,114.4
N	3	143,838.0	143,859.4
N (nitro)	3	143,887.9	143,908.2
N	2	143,843.4	143,856.5
N	1	143,856.7	143,846.6
O	2	197,416.2	197,426.1
O	1	197,418.1	197,427.9
F	1	262,037.0	262,042.9
Cl	1	1,208,407.3	1,208,399.3

planar increment is puzzling. Therefore, such a distinction is avoided here. In fact, the present study indicates that the trouble originates from the nitro groups. Indeed, introducing a special AE for nitrogen in  $-\text{NO}_2$  proves very useful. Although this equivalent was obtained from a set of only four nitroalkanes, we are confident in its significance because the regression yielded a correlation coefficient very close to unity. The value thus obtained for the AE is 50 kJ/mol larger than the normal value for other trivalent nitrogen atoms, no matter what procedure is considered. The lower difference of 33 kJ/mol reported previously between correction terms associated with planar and pyramidal trivalent nitrogens might result from the fact that the nitrogen in  $-\text{NO}_2$  was treated on the same ground as planar nitrogens in groups such as amides,<sup>26</sup> for which the value associated with pyramidal nitrogens actually seems more suitable.

In fact, for both P1 and P2 protocols, the special case of nitro groups shows that environment-dependent AEs are mandatory for nitrogen compounds at the BP/DN<sup>†\*</sup> level. In light of these results, it would be interesting to investigate the transferability of the nitrogen AE for higher levels of theory. Notwithstanding the pathological case of nitros, the AEs do not significantly depend on the chemical environment of the atoms or their hybridization (Table III). Nonetheless, it might be interesting to note that the lower the coordination number of an atom, the higher the associated  $X_K$  value, although this rule does not emerge from the earlier correction terms developed for

DFT energies.<sup>26</sup> In fact, there is generally no obvious correlation between the  $X_K$  listed in Table III and the corresponding correction terms reported previously. In addition to the use of MMFF and of a higher quality basis set, this may be due to the different calibration panels employed. Furthermore, some of the AEs associated with the HGCMP method were obtained from a single equation. For instance, the correction term for monovalent nitrogen was derived from acetonitrile only. Because the optimal value for this particular molecule may not be suitable in general for predicting  $\Delta_f H^\circ$  of other molecules showing *sp* nitrogen, we tried to average the AEs with respect to chemical environments through deriving each value from several molecules (Table II). Unfortunately, in some cases this averaging was hampered by a lack of reliable data. In particular, while the AE for nitrogen in nitros is meant to be used for any nitro group whatever its chemical environment, the value reported in Table III is obtained from nitroalkanes data only.

## Formation Enthalpies



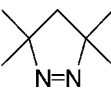
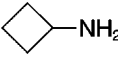

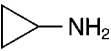
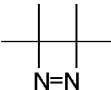
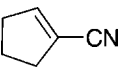

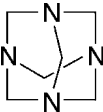
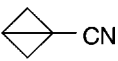
### GENERAL DISCUSSION

Both sets of AEs were applied to the calibration panel (Table II) and to more than 100 additional test molecules including the HGCMP panel. The explicit calculation of zero-point and thermal energies, as done in the P1 procedure, does not improve the results with respect to the simpler P2 procedure. This fact had already been noticed in the context of molecular mechanics by Allinger and coworkers who showed that the experimental enthalpies can be accurately reproduced without any explicit dependence on the vibrational frequencies.<sup>12-17</sup> Moreover, considering the values of the increments of the HGCMP scheme,<sup>26</sup> it is clear that the explicit calculation of  $\Delta_f H^\circ$  in terms of the frequencies does not alleviate the need for significant corrections. Thus, the accuracy of the P2 procedure is limited by the AE scheme and the DFT model employed rather than by the inclusion of zero-point energies and temperature-dependent terms in the AEs. Because both P1 and P2 protocols yield very similar results, the following discussion focusses on the P2 results, although most considerations also hold true for P1 enthalpies.

For hydrocarbons, the rms error of the P2 procedure is 8.6 kJ/mol. By comparison, the recent study of Mole et al.<sup>27</sup> reports rms errors ranging from 4.3 to 10.5 kJ/mol for a set of 23 small



**TABLE IV.**  
Results Obtained through the P2 Procedure for Strained Molecules, Compared with Experiment (kJ/mol).

	<i>Exp.</i> <sup>42</sup>	P2
	-80.5	-95.7
	28.4	20.2
	39.3	46.9
	41.2	62.3
	53.1	42.5
	77.0	75.8
	150.3	160.1
	156.4	149.4
	182.8	167.1
	199.0	227.7
	304.5	343.1
rms error		18.1

and stable hydrocarbons, according to the functional used (notwithstanding the very poor results obtained within the local spin density approximation). Although it is based on a more approximate functional, the present scheme involves three different AEs for carbon according to its coordination number (Table III). This is probably the reason for its relatively good performance. Because they consider only the hybridization of the atoms, present approaches handle all hydrocarbons on the same footings. In particular, the P2 results for alkanes, showing a rms error of 9.4 kJ/mol, are not better than for unsaturated hydrocarbons. Better results can probably be obtained if additional group equivalents are obtained. Indeed, using true DFT energies and introducing eight group and bond equivalents, Labanowski et al. were able to fit formation en-

thalpies of a panel of 52 alkanes with a rms error of 1.6 kJ/mol.<sup>29</sup>

For other classes of compounds including alcohols, ketones, aldehydes, ethers, carboxylic acids, nitriles, and halogenated hydrocarbons, the deviations from experiment are typically in the range 10–15 kJ/mol. In view of previous results,<sup>24, 26–29</sup> this loss of accuracy does not appear to be associated with the use of MMFF structures. Indeed, despite the excellent results reported for hydrocarbons,<sup>24, 27, 29</sup> general methods either use more adjustable parameters<sup>23</sup> or show only a fair accuracy not superior to the present results.<sup>26, 28</sup> It is gratifying to note that in most cases, the present procedures yield satisfactory results with regard to strained compounds shown in Table IV (for which group contribution methods should have trouble), despite an error close to 40 kJ/mol for bicyclo[1.1.0]butane-1-carbonitrile.

As far as nitrogenous compounds are concerned, large errors are observed, the most significant ones using the P2 procedure being observed for 1,3,5-trinitrobenzene (81 kJ/mol), 1,3-dinitrobenzene (56 kJ/mol), TATB (50 kJ/mol), tetrazole (42 kJ/mol), methyl-nitrate (36 kJ/mol), methyl-nitrite (34 kJ/mol), and dimethylfurazan (31 kJ/mol). Those results are expected in view of the problems mentioned above with regard to the molecular mechanics parameterization of such compounds. There is no doubt that the use of MMFF structures does introduce a significant source of error in those particular cases. For nitroethylene and nitroaromatic compounds, the rms error is reduced from ca. 50 kJ/mol to ca. 30 kJ/mol if planarity is imposed. Meanwhile, the largest error is reduced from 81 kJ/mol (for 1,3,5-trinitrobenzene) to 50 kJ/mol (for TATB).

## COMPARISON WITH OTHER METHODS

In Table V, the formation enthalpies calculated for the HGCMP panel using the present procedures are compared with the results of the HGCMP method. PIMM values are also reported to illustrate the improvement on going from semiempirical to first-principles energy calculations. Because this comparison bears on the HGCMP panel, it confers an advantage on the HGCMP method.

The PIMM model yields a rms error of 30.1 kJ/mol, comparable to the rms error of 32.3 kJ/mol obtained using PM3. However, no value is obtained from PIMM for allene owing to a lack of parameters for the central carbon. On the other hand,  $\Delta_f H^\circ$  of dimethylfuroxan is not

**TABLE V.**   
**Formation Enthalpies for the Compounds Studied in Ref. 26 (kJ/mol).**

	Exp. <sup>42</sup>	PIMM	P1	P2	HGCMP <sup>26</sup>
Chlorodifluoromethane	−482.0	−438.6	−472.6	−485.9	−461.7
Methyl acetate	−411.5	−412.9	−423.3	−426.9	−405.6
Ethylene glycol	−387.1	−411.1	−374.0	−386.1	−357.9
Formic acid	−378.6	−371.8	−385.7	−392.7	−352.8
1,4-Dioxane	−315.5	−307.2	−296.5	−300.8	−332.8
1-Fluoropropane	−285.6	−285.1	−293.1	−296.2	−272.8
Diethyl ether	−251.8	−253.0	−268.7	−267.2	−265.1
Urea	−245.6	−211.4	−234.9	−241.6	−211.3
Water	−241.6	−234.3	−227.9	−233.8	−197.8
Acetamide	−238.1	−214.0	−248.3	−251.3	−224.5
Ethanol	−235.0	−242.1	−233.3	−240.7	−219.6
Acetone	−217.1	−209.7	−224.1	−223.2	−196.3
Methanol	−201.3	−219.6	−197.9	−204.5	−183.6
Dimethylether	−183.9	−208.0	−189.9	−195.3	−184.7
Neopentane	−168.0	−175.0	−169.0	−167.3	−154.5
<i>n</i> -Butane	−125.5	−127.9	−132.6	−134.3	−127.3
Methyl nitrate	−122.1	−189.9	−154.0	−158.2	−163.9
Chloroethane	−112.0	−100.8	−108.1	−120.3	−117.9
Formaldehyde	−108.5	−120.8	−108.8	−107.8	−79.8
Propane	−104.6	−106.2	−113.4	−114.0	−105.8
Nitroethane	−102.2	−121.8	−115.5	−116.7	−84.1
Ethane	−83.6	−85.6	−91.4	−90.9	−84.7
Nitromethane	−74.4	−97.2	−87.3	−86.9	−46.8
Methane	−74.4	−65.3	−78.8	−75.4	−70.6
Methyl nitrite	−66.5	−81.6	−30.0	−32.2	−81.0
Ammonia	−46.0	−9.4	−41.8	−42.7	−22.9
Benzaldehyde	−36.7	−45.1	−40.7	−45.3	−40.6
Furan	−34.9	−61.7	−26.0	−42.5	−54.2
Methylamine	−23.0	−23.5	−22.9	−24.7	−14.3
Isobutene	−16.9	−2.7	−14.8	−15.9	−11.0
Oxazole	−15.5	−40.6	−11.7	−29.7	−16.7
Dimethylnitramine	−4.6	30.1	−26.7	−26.3	−11.2
Propene	20.0	28.1	22.2	20.5	26.6
Vinyl chloride	37.2	20.8	36.4	22.3	14.3
Nitroethylene	37.6	2.0	45.0	41.0	59.4
4,5-dihydro-3-nitroisoxazole	39.0	−34.8	28.0	53.1	50.0
Chlorobenzene	51.8	52.4	64.1	50.4	39.3
TATB	51.8	−34.8	101.7	102.0	75.0
Ethylene	52.3	59.5	59.1	57.7	65.3
Cyclopropane	53.1	50.3	29.0	42.5	50.9
1,3-Dinitrobenzene	53.9	24.9	67.2	65.6	71.4
1,4 Dinitropiperazine	58.1	155.0	29.3	35.9	50.6
4-Nitroaniline	58.9	34.6	87.3	83.6	54.0
1,3,5-Trinitrobenzene	62.3	46.5	81.1	80.0	76.2
Acetonitrile	64.4	87.9	81.6	62.0	64.2
Nitrobenzene	67.3	37.1	66.1	63.5	68.1
Isoxazole	78.6	104.4	69.9	55.4	64.7
Benzene	82.3	82.5	83.6	79.9	79.2
Aniline	86.9	90.2	85.5	80.7	77.9
Methylhydrazine	94.5	91.7	85.5	85.3	87.6
Dimethylfuroxan	102.2	123.9			68.6
Dimethylfurazan	107.2	160.4	80.8	76.0	82.6
Pyrrole	108.2	74.4	104.2	100.3	101.4

**TABLE V.**  
(Continued)

	Exp. <sup>42</sup>	PIMM	P1	P2	HGCMP <sup>26</sup>
1,3-Butadiene	109.9	110.4	122.2	116.4	118.9
Pyridine	140.3	153.9	131.5	128.1	131.2
Indole	156.3	169.5	158.2	154.7	139.1
Propyne	184.7	185.1	184.3	185.0	178.2
Allene	190.3		177.7	183.0	188.4
RDX	191.4	240.7	178.7	185.1	167.6
Pyrimidine	195.7	203.5	174.1	171.1	196.9
Pyrazine	195.9	212.1	188.3	186.1	212.1
Acetylene	228.0	227.1	240.0	240.1	234.5
Pyridazine	278.1	284.3	258.7	258.4	282.2
Tetrazole	334.2	359.7	290.6	292.5	332.1
rms abs. deviation		28.7	15.7	15.5	17.1
maximum abs. deviation		96.9	59.6	64.8	43.8

estimated using the present procedures because of a lack of experimental data to determine a suitable AE for the monovalent *sp* oxygen atom. According to the rms errors, the P1 and P2 procedures are significantly more reliable than both PIMM and PM3 models. Interestingly enough, the rms errors for P1 and P2 are comparable to that obtained using the much more costly HGCMP procedure,<sup>26</sup> despite the poor MMFF geometries and severe errors (as large as 80 kJ/mol) for molecules with C(*sp*2)—NO<sub>2</sub> groups. Indeed, both P1 and P2 yield rms errors below 16 kJ/mol, to be compared with the HGCMP value of 17 kJ/mol. Present results are even better if the planarity of the C(*sp*2)—NO<sub>2</sub> groups is imposed during the MMFF optimization.

### STATUS OF THE P2 PROCEDURE

Despite its usefulness with regard to energetic materials, the P2 procedure is crude compared with more specific techniques such as the MM3 force

field. However, in some cases, some experimental values of  $\Delta_f H^\circ$  cannot be fitted using the MM3 procedure, even for molecules without unusual structural features,<sup>15,16</sup> such as those listed in Table VI. In most cases, this puts some doubts on the experimental data. Nevertheless, the experimental  $\Delta_f H^\circ$  value for 3,4-benzoquinoline to which the MM3 results were compared<sup>15</sup> have been confirmed by Steele et al.<sup>56</sup> It is lower than the MM3 calculated value by at least 23 kJ/mol. This suggests that predicting  $\Delta_f H^\circ$  within a few kJ/mol without resorting to time-consuming *ab initio* procedures is very difficult, even for simple organic compounds. No surprisingly, the results in Table VI are even worse for the PIMM model. On the other hand, the results obtained using the P2 procedure are consistent with the data reported above. In principle, as long as the molecules studied remain within the scope of the MMFF force field, no dramatic error should arise unless very large molecules are considered.

**TABLE VI.**  
Formation Enthalpies Predicted by MM3 and the P2 Scheme (kJ/mol).

Molecule	MM3	PIMM	PM3	P2	Exp.
3,4-Benzoquinoline	267.7	274.3	255.7	266.1	243.3 <sup>a</sup> ; 240.5 ± 4.2 <sup>b</sup>
5,6-Benzoquinoline	267.7	269.7	259.8	267.4	233.7 ± 7.4 <sup>a</sup>
7,8-Benzoquinoline	267.2	269.6	261.7	258.4	230.7 <sup>a</sup> ; 250.4 ± 2.3 <sup>b</sup>
2-Vinylfuran	14.2	−9.8	53.0	18.0	27.8 ± 4 <sup>c</sup>

<sup>a</sup> Ref. 15.

<sup>b</sup> Ref. 56.

<sup>c</sup> Ref. 59.

Being more reliable than semiempirical methods, the P2 procedure is a valuable alternative to previous schemes based on DFT only, affording dramatic savings of CPU time with no significant loss of accuracy. Nevertheless, it is likely to fail for unusual compounds or small molecules showing unique bonding such as hydrogen fluoride, owing to some breakdowns of the extended MMFF parameterization. As an example of application of this method, the solid-state formation enthalpies compiled in the ICT database<sup>57</sup> have been recently estimated, excluding nitroaromatic compounds.<sup>58</sup> The sublimation enthalpies were obtained through a new method based on recent investigations.<sup>3</sup> The rms error was 0.17 MJ/kg using the P2 procedure for the gas-phase contribution vs. 0.25 MJ/kg using semiempirical methods (PM3, PIMM).<sup>58</sup> In view of the available experience with the use of AEs, it is clear that more accurate results could be obtained using group equivalents whenever useful, for example, for nitro, nitrates, nitramines, azo compounds, etc.

## Conclusion

Although this article presents cost-effective methods to predict  $\Delta_f H^\circ$  for organic compounds, its main interest stems from the guidelines it suggests for further developments. In particular, it appears that combining molecular mechanics (to optimize the geometry) with quantum chemistry (to calculate the energy) may be fruitful, although the high accuracy reported for recent force fields such as MMFF still remains to be extended beyond the biochemical field.

With regard to the future of AE-based approaches to formation enthalpies, two directions may be foreseen. On one hand, methods employing only one AE for each chemical element are needed to investigate enthalpy changes during reactive processes, as pointed out by Dewar and O'Connor.<sup>25</sup> In this context, high-quality models of the electronic structure should be useful in view of the better performance of B3LYP over more approximate functionals.<sup>27</sup> On the other hand, to estimate  $\Delta_f H^\circ$  for stable molecules, the use of molecular mechanics affords dramatic time savings with respect to conventional approaches, which means that more and/or larger systems can be investigated. For such methods, the use of different AEs according to the chemical environment of the atoms is consistent with the variety of atom types involved in force fields definitions, and should make it possible to take advantage of

lower levels of theory. In the short run, there is a need to investigate the scope of present force fields and to identify the limitations of empirical rules employed to calculate parameters for bond stretching, angle bending, and torsions in terms of atomic parameters. Then, further investigations will be required to define the optimal combinations, namely: force field + electronic structure model + set of AEs.

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